

ABSTRACT OF THE DISCLOSURE

1 Methods for the preparation of a lipid-nucleic acid composition are provided.
2 According to the methods, a mixture of lipids containing a protonatable or deprotonatable lipid,
3 for example an amino lipid and a lipid such as a PEG- or Polyamide oligomer-modified lipid is
4 combined with a buffered aqueous solution of a charged therapeutic agent, for example
5 polyanionic nucleic acids, to produce particles in which the therapeutic agent is encapsulated in a
6 lipid vesicle. Surface charges on the lipid particles are at least partially neutralized to provide
7 surface-neutralized lipid-encapsulated compositions of the therapeutic agents. The method
8 permits the preparation of compositions with high ratios of therapeutic agent to lipid and with
9 encapsulation efficiencies in excess of 50%.